

molecules and thereby induces an HLA-B-restricted cytotoxic T cell response, said method comprising steps of:

- providing an amino acid sequence of an antigen of interest;
- identifying a putative T cell epitope within said amino acid sequence, whereby said putative epitope comprises a structural B7 supermotif associated with peptide binding to multiple HLA-B molecules, said structural supermotif comprising an amino acid residue P at position two from an N-terminal residue of the epitope, and a residue selected from the group consisting of V, I, L, F, M, W, Y, and A at a carboxyl-terminus of the epitope;
- obtaining one or more peptide fragments of the amino acid sequence that comprise the HLA B7 structural supermotif;
- testing a first complex of said one or more peptide fragments and a first HLA-B molecule for an ability to be recognized by HLA-B-restricted cytotoxic T cells and to thereby induce a cytotoxic T cell response to the epitope;
- testing at least a further complex of said one or more peptide fragments and at least a second HLA-B molecule for an ability to be recognized by HLA-B-restricted cytotoxic T cells and to thereby induce a cytotoxic T cell response to the epitope; and,
- selecting said one or more peptide fragments comprising an HLA-B7 structural supermotif that induce a cytotoxic T cell response to the epitope when the epitope is in the first complex and the second complex.

17. The method of claim 16 wherein the identifying step comprises identifying a peptide fragment from a cancer-associated antigen.

18. The method of claim 17 wherein the identifying step comprises identifying a peptide fragment from an antigen that is HER2/neu.

19. The method of claim 17 wherein the identifying step comprises identifying a peptide fragment from an antigen that is p53.

20. The method of claim 17 wherein the identifying step comprises identifying a peptide fragment from an antigen that is a MAGE antigen.

21. The method of claim 17 wherein the identifying step comprises identifying a peptide fragment from an antigen that is a prostate antigen.

22. The method of claim 16 wherein the identifying step comprises identifying a peptide fragment from an antigen that is derived from a pathogenic agent.

23. The method of claim 22 wherein the identifying step comprises identifying a peptide fragment from an antigen that is HIV.

24. The method of claim 22 wherein the identifying step comprises identifying a peptide fragment from an antigen that is HBV.

25. The method of claim 22 wherein the identifying step comprises identifying a peptide fragment from an antigen that is HCV.

26. The method of claim 22 wherein the identifying step comprises identifying a peptide fragment from an antigen that is a malaria antigen.

27. The method of claim 16, wherein the peptide fragment has 8, 9, 10 or 11 residues.

28. The method of claim 16, wherein the peptide fragment has at least 15 residues.

29. The method of claim 16, wherein at least two peptide fragments are obtained.

30. The method of claim 16, further comprising a step of:
determining binding affinity of the peptide fragment for an HLA-B molecule.
31. The method of claim 30, further comprising a step of identifying a
peptide fragment that has an IC_{50} for an HLA-B molecule of less than about 500 nM.
32. The method of claim 30, wherein the step of determining binding
affinity comprises:
determining binding affinity of a peptide fragment for an HLA-B molecule that
is an HLA-B7 supertype molecule.
33. The method of claim 16, wherein the obtaining step comprises isolation
of the one or more peptide fragments from a natural source.
34. The method of claim 16, wherein the obtaining step comprises synthesis
of a peptide fragment.
35. The method of claim 34, wherein the synthesis comprises chemical
synthesis.
36. The method of claim 16, wherein the obtaining step comprises
expressing a recombinant nucleic acid molecule that encodes the peptide fragment.
37. The method of claim 36, wherein the obtaining step comprises
expressing a recombinant nucleic acid molecule that encodes the peptide fragment and at least
one additional peptide, with a *proviso* that an additional peptide is not an entire native antigen.
38. The method of claim 16, wherein the obtaining step comprises obtaining
a longer peptide comprising the peptide fragment, with a *proviso* that the longer peptide is not
an entire native antigen.

39. The method of claim 16, wherein the testing step occurs *in vitro*.
40. The method of claim 16, wherein the testing step occurs *in vivo*.
41. A method of making a peptide that binds to an HLA-B molecule at a level of affinity predicted to be immunogenic in humans, said method comprising steps of:
- a) obtaining a peptide that comprises an epitope consisting of about 8-11 residues, the epitope comprising an amino acid P at a position two relative to an amino terminus of the epitope, and V, I, L, F, M, W, Y, or A at a carboxyl terminus of the epitope;
 - b) determining binding affinity of the peptide for at least two different HLA-B molecules; and,
 - c) selecting a peptide of step b) that comprises an IC₅₀ for at least two HLA-B molecules of less than about 500 nM.
42. The method of claim 41 wherein the obtaining step comprises expressing a nucleic acid sequence that encodes the peptide.
43. The method of claim 42, wherein the obtaining step comprises expressing a nucleic acid sequence that encodes the peptide and at least one additional peptide, with a *proviso* that an additional peptide is not an entire native antigen.
44. The method of claim 41, wherein the obtaining step comprises obtaining a longer peptide comprising the peptide, with a *proviso* that the longer peptide is not an entire native antigen.
45. The method of claim 41 wherein the obtaining step comprises obtaining a peptide of 8, 9, 10 or 11 amino acids in length.

46. The method of claim 41 wherein the obtaining step comprises obtaining a peptide of at least 15 amino acids in length.

47. The method of claim 41 wherein the determining step comprises determining binding affinity of the peptide for an HLA-B molecule that is an HLA B7 supertype molecule.

48. The method of claim 41, wherein the obtaining step comprises isolation of the peptide from a natural source.

49. The method of claim 41, wherein the obtaining step comprises synthesis of the peptide.

50. The method of claim 49, wherein the synthesis comprises chemical synthesis.

51. A method of making a peptide that binds to an HLA-B molecule at an IC_{50} less than about 500 nM, the method comprising the steps:

(a) providing an amino acid sequence having an amino terminus and a carboxyl terminus;

(b) identifying a putative T cell epitope from the provided amino acid sequence, whereby said putative epitope consists of about 8-11 residues and comprises a B7 supermotif associated with peptide binding to an HLA-B molecule, said supermotif comprising a first amino acid residue at position two from an N-terminal residue of the epitope, said first residue selected is P, and a residue selected from the group consisting of V, I, L, F, M, W, Y, and A as a carboxyl-terminal amino acid of the epitope;

(c) obtaining a peptide comprising the putative epitope identified in step (b), with a *proviso* that the obtained peptide does not comprise an entire native antigen;

(d) determining binding affinity of the peptide for at least two different HLA B molecules; and,

(e) selecting a peptide having an IC_{50} of less than about 500 nM for at least two different HLA-B molecules.

52. The method of claim 51, further comprising a step of:

(f) contacting an HLA-B-restricted cytotoxic T lymphocyte with a complex of the peptide of step (e) and an HLA-B molecule.

53. The method of claim 51 wherein the amino acid sequence is derived from a cancer-associated antigen.

54. The method of claim 53 wherein the amino acid sequence is derived from an antigen that is HER2/neu.

55. The method of claim 53 wherein the amino acid sequence is from an antigen that is p53.

C 56. The method of claim 53 wherein the amino acid sequence is from an antigen that is a MAGE antigen.

57. The method of claim 53 wherein the amino acid sequence is from an antigen that is a prostate antigen.

58. The method of claim 51 wherein the peptide is derived from an antigen that is derived from a pathogenic agent.

59. The method of claim 58 wherein the amino acid sequence is derived from an antigen that is HIV.

60. The method of claim 58 wherein the amino acid sequence is derived from an antigen that is HBV.

61. The method of claim 58 wherein the amino acid sequence is derived from an antigen that is HCV.

62. The method of claim 58 wherein the amino acid sequence is derived from an antigen that is a malaria antigen.

63. The method of claim 51, wherein the contacting step occurs *in vitro*.

64. The method of claim 51, wherein the contacting step occurs *in vivo*.

65. The method of claim 51 for making a peptide that binds to an HLA-B molecule at an IC_{50} less than about 500 nM, wherein step (b) comprises:

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(b) identifying a putative T cell epitope from a polypeptide antigen, whereby said putative epitope comprises a B7 supermotif associated with peptide binding to an HLA-B molecule, said supermotif comprising a first amino acid residue at position two from an N-terminal residue of the B7 supermotif, said first residue is P, and a residue selected from the group consisting of V, I, L, F, M, W, Y, and A as a carboxyl-terminal amino acid of the B7 epitope.

66. The method of claim 65 wherein steps (d) and (e) comprise:

(d) determining binding affinity of the peptide for an HLA-B7 supertype molecule; and,

(e) selecting a peptide having an IC_{50} of less than about 500 nM for the HLA-B7 supertype molecule.--

REMARKS

With this amendment, Applicants request entry of new claims 16-66 in the patent application. These claims replace originally filed claims 1-15. Thus, the request for